IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Title	:	Novel Flow Cytometer			
Inventor	:	Glenn F. Spaulding			
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APPEAL BRIEF

This is an appeal from the final rejection of claims 1-4, 10, 11, 13-31, 33 and 34 dated 6 October 2003.

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REAL PARTY IN INTEREST

The real party in interest in the above-identified application is Spin Diagnostics, Inc. of Houston, Texas. Assignment to Spin Diagnostics, Inc. was recorded in the Patent Office on 18 June 2002 at Reel/Frame 013012/0015.

RELATED APPEALS AND INTERFERENCES

To the present knowledge of Appellant's representative, there are currently no related appeal or interference proceedings that will directly affect, be directly affected by, or have a bearing on, the Board's decision in the present Appeal.

STATUS OF CLAIMS

Claims 1-4, 10, 11, 13-31, 33 and 34 are currently pending. Claims 1-4, 10, 11, 13-31, 33 and 34 have been finally rejected under 35 U.S.C. 112, second paragraph. Claims 1, 3, 4, 10, 11, 13-18, 22, 24-31, 33 and 34 have been finally rejected under 35 U.S.C. 103(a) as being unpatentalbe over Cottingham (US 5,639,428) in view of Walters (US 6,135,940). Claims 1, 4, 10, 13-18, 22, 26-29, 31, 33 and 34 have been finally rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson (US 6,254,834) in view of Walters. Claims 19, 20 and 23 have been finally rejected under 35 U.S.C. 103(a) as being unpatentable over Cottingham or Anderson in view of Walters. Claims 2 and 21 have been finally rejected under 35 U.S.C. 103(a) as being unpatentable over

Cottingham or Anderson in view of Walters and further in view of Saralegui (US 5,439, 645).

STATUS OF AMENDMENTS

No amendments have been filed responsive to the Examiner's Final Office Action dated 6 October 2003.

SUMMARY OF INVENTION

The invention is directed to a "a novel flow cytometer ... [in which a] ... container, upon centrifugation, directs and enables the movement of cells, which have been placed in the container, towards the outer walls of the container. A light source and photodetector external to the rotating container interrogates the cells located inside of the container on the outer wall ... Said apparatus and methods of interrogating said cells yield information on cell location, size, shape, cellular constituents, cell volume, and cell buoyancy; and when labeled with a fluorescent or other marker, specific cellular constituents, cell function, and genomic information ... Analysis is accomplished in a sealed disposable container." (Specification at page 1, lines 7-23. See also page 3, lines 2-19. All references herein to the "Specification" are to the substitute specification filed by Appellant on 15 August 2002 and acknowledged by the Examiner in her Office Action dated 12 November 2002.)

In the illustrative embodiment of the claimed cytometric apparatus shown in Figure 1, a "cylinder or container having an open end and a closed end **2** has a cell

guide **3** inserted into the cylinder ... The cylinder **2** is vertically rotated by a motor means **5** ... that would allow rotation around the vertical axis of cylinder **2**. A light source **9** such as an LED or laser and a photodetector **8** are adapted to interrogate cells that are dispersed to the inner surface of the wall of cylinder **2** during centrifugation. The light source **9** and photodetector **8** are disposed to a linear motion means for vertical up/down movement **6** with shaft **7** by means **10**; means **10** is adapted to precisely position the light source **9**/photodetector **8** with respect to the cylinder **2** ... Alternatively, the linear motion means are adapted to vertically move said rotating cylinder while the photodetectors and light sources remain in a fixed position." (Specification at page 5, lines 2-20 and Figure 1.)

Illustrative embodiments describing how the apparatus of Figure 1 may be constructed and used, including specific and enabling identification of the claimed components of the apparatus are set forth in eighteen (18) separate examples. For example, illustrative details of the claimed cylinder **2** and its associated cap **1** and cell guide **3** are discussed in examples 1 (Specification at page 5, line 22 to page 6, line 2), 2 (Specification at page 6, lines 4-12), 16 (Specification at page 11, lines 22-28) and 18 (Specification at page 12, lines 14-24). See also, page 3, lines 3-19. Similarly, illustrative details of photodetector **8** and light source **9** are described in examples 1 (Specification at page 5, line 22 to page 6, line 2), 3 (Specification at page 6, lines 14-17), 9 (Specification at page 7, line 24 to page 8, line 6), 11 (Specification at page 8, line 20 to page 9, line 9) and 15 (Specification at page 10, line 25 to page 11, line 20). See also, page 3, lines 20-29. In addition, motion means **6** and means **10** for precisely

positioning photodetector **8**/light source **9** are described in examples 1 (Specification at page 5, line 22 to page 6, line 2), 2 (Specification at page 6, lines 4-12) and 16 (Specification at page 11, lines 22-28). See also, page 3, lines 20-28 and page 4, lines 1-11. Further, illustrative analysis means are described in examples 4 (Specification at page 6, lines 19-25), 5 (Specification at page 6, lines 27-30), 12 (Specification at page 9, line 11 to page 10, line 8), 13 (Specification at page 10, lines 10-17), 14 (Specification at page 10, lines 19-23), 15 (Specification at page 10, line 25 to page 11, line 20), and 17 (Specification at page 12, lines 1-12). See also, page 1, lines 17-22 and page 4, lines 1-11.

In summary, the claimed invention is directed to an apparatus that employs one or more light sources (e.g., lasers), one or more light detectors (e.g., photomultiplier tubes), mechanical motion devices (e.g., stepper motors) and well-known analysis techniques for the purpose of determining known cytometric characteristics of the media being interrogated (e.g., "size, shape, cellular constituents, cell volume, and cell buoyancy; and when labeled with a fluorescent or other marker, specific cellular constituents, cell function, and genomic information," see Specification at page 1, lines 13-16).

Applicant's central contribution to the art is the recognition and exploitation of the fact that cytometric analysis of a sample may be performed in a closed container rotating about its longitudinal axis. No known prior art teaches, describes or fairly suggests this concept. As would be recognized by even a casual practitioner in the field of cytometric analysis in general, and flow cytometry in particular, the use of a light

source and the capture of reflected and or transmitted light energy from the sample are fundamental and well understood principles that are central to the operation of any flow cytometric device.

In accordance with this recognition, noted benefits of the claimed apparatus include the elimination of a traditional flow cytometer's "complicated system of pressure containers, valves, sheath fluid flows, orienting nozzles and other assorted equipment to move cells in single file through a gas laser light source" all of which add complexity and expense when compared to a cytometric device in accordance with the claimed invention. (Specification at page 1, lines 27 to page 2, line 8.) That is, "[c]ylinder rotation provides a novel integrated means that accomplishes cell orientation, cell localization, cell containment within a simple to manufacture and disposable container." (Specification at page 2, lines 19-21.) Another noted benefit is the claimed device's extremely high cell analysis rates (in excess of 1,000,000 cells/second) compared to the prior art flow cytometric technology. (Specification at page 4, lines 17-19.) A further benefit, one that would be understood by those in the field of flow cytometry and, in particular, those involved with the use of prior art flow cytometer devices, is the increased level of personal safety when performing cytometric analysis using the claimed apparatus – a direct result of using a closed rotating cylinder rather than an open fluid flow stream.

ISSUES

A total of 27 claims are pending (1-4, 10, 11, 13-31, 33 and 34), of which 2 are independent (1 and 10). The following issues comprise the issues at bar:

1. Whether the term "adapted" is indefinite under 35 U.S.C. 112, second paragraph, to one of ordinary skill in the art of flow cytometry and cytometric analysis.
   a) Claim 1: "detector adapted to detect."
   b) Claims 1 and 10: "a rotating means adapted to rotate."
   c) Claims 1, 10, 26: "a light source adapted to illuminate."
   d) Claim 2: "barcode adapted to be interrogated."
   e) Claim 11: "a rotating means further adapted to sequentially rotate."
   f) Claim 13: "a cap adapted to seal the open end."
   g) Claims 23, 27: "light emitting diode adapted to emit."
2. Whether the phrase "cytometric characteristic of a sample" is indefinite under 35 U.S.C. 112, second paragraph, to one of ordinary skill in the art of flow cytometry and cytometric analysis. (Independent claim 1.)
3. Whether 35 U.S.C. 112, second paragraph, requires individual dependent claims to be "functionally" related when they do not depend from one another. (Dependent claims 3 and 4.)
4. Whether the Examiner properly rejected the claimed "an analog digital converter" as an improper antecedent basis under 35 U.S.C. 112, second paragraph. (Dependent claim 25.)

5. Whether the claimed invention is patentable under 35 U.S.C. 103 over US patent 5, 639, 428 to Cottingham (hereinafter, Cottingham) in view of US patent 6,135,940 to Walters (hereinafter, Walters). (Independent claims 1 and 10. Dependent claims 3, 4, 11, 13-18, 22, 24-31, 33 and 34.)

6. Whether the claimed invention is patentable under 35 U.S.C. 103 over US patent 6,254,834 to Anderson et al. (hereinafter, Anderson) in view of Walters. (Independent claims 1 and 10. Dependent claims 4, 13-18, 22, 26-29, 31, 33 and 34.)

7. Whether the claimed invention is patentable under 35 U.S.C. 103 over Cottingham or Anderson in view of Walters and further in view of Surmodics, Inc. (Dependent claims 19, 20 and 23.)

8. Whether the claimed invention is patentable under 35 U.S.C. 103 over Cottingham or Anderson in view of Walters and further in view of US patent 5,439,645 to Saralegui et al. (hereinafter, Saralegui). (Dependent claims 2 and 21.)

GROUPING OF CLAIMS

Claims 1-4 stand or fall together.

Claims 10, 11, 13-31, 33 and 34 stand or fall together.

ARGUMENTS

A. The Term "Adapted" is Not Indefinite to One of Ordinary Skill in the Art of Flow Cytometry and Cytometric Analysis

It is long established that the purpose of a claim is to define the invention, not to explain it. *See Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1575-76 (Fed. Cir. 1986) (a claim need not "describe" the invention, such description being the role of the disclosure). As for the level of specificity required to meet the requirements of section 112, if "the claims, read in the light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention ... the courts can demand no more." *Shatterproof Glass Corp. v. Libbey-Owens Ford Co.*, 758 F.2d 613, 624 (Fed. Cir.), *cert dismissed*, 474 U.S. 976 (1985); *United States v. Telectronics, Inc.*, 857 F.2d 778, 786 (Fed. Cir. 1988), *cert. denied*, 490 U.S. 1046 (1989); *Hybritech, Inc. v. Monoclonal Antibodies, Inc*, 802 F.2d 1367, 1385 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); M.P.E.P. 706.03(d). That is, a claim is distinct if those of ordinary skill in the art understand its meaning. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1378-1379 (Fed. Cir. 2000).

Thus, the acceptability of an Applicant's claim language depends upon whether one of ordinary skill in the art would understand what is claimed in light of the specification, and not whether the Examiner subjectively believes there is a "better way" to express the Applicant's intent. M.P.E.P. 2173.01 (applicants may use "whatever

terms they choose so long as those terms are not used in ways that are contrary to accepted meanings in the art").

With respect to the specification, Appellant submits that each of the allegedly indefinite phrases are described in such clear and concise language as to be immediately understood by any person with even a passing knowledge of cytometric principles. Specifically:

a. Claim 1: "detector adapted to detect." Several embodiments using different types of detectors are described within the specification, such as at Example 15 at page 10, lines 26-30. See also: page 3, lines 20-28; page 5, lines 10-13; Example 1 at page 5, lines 25-28; Example 3 at page 6, lines 15-17; Example 9 at page 7, line 29 to page 8, line 6; and Example 11 at

b. Claims 1 and 10: "a rotating means adapted to rotate." Several embodiments using various rotating means are described within the specification. See, for instance, FIG. 1 and its discussion at page 5, lines 2-20. See also Example 1 at page 5, lines 23-25.

c. Claims 1, 10, 26: "a light source adapted to illuminate." Several embodiments using different types light sources are described within the specification, such as at Example 15 at page 11, lines 1-4. See also: page 2, lines 16-18; page 3, lines 20-28; page 5, lines 10-13; and Example 1 at page 5, lines 23-24.

d. Appellant further contends that any person having even a passing knowledge of flow cytometric principles would comprehend that various light sources (e.g., having different wavelengths) may be selected (e.g., adapted) depending upon

the cytometric characteristic being measured. This is evidenced by the following table taken from an introductory text of Flow Cytometry principles and provided to the Examiner in Appellant's Reply filed 29 January 2003.

Laser type	Wavelengths (nm)	Possible fluorochromes
Argon ion	488	Fluorescein, R-phycoerythrin, PerCP, PE-tandems, EGFP, EYFP, propidium iodide, Alexa 488, acridine orange
	514	Rhodamine, propidium iodide, EYFP, R-phycoerythrin
	Ultraviolet (351/364)	Hoechst dyes, DAPI, Indo-1, AMCA, Cascade Blue, EBFP
Helium-neon (HeNe)	Usually 633	Allophycocyanin, Cy5, TO-PRO-3
Krypton ion	568	Cy3, Texas Red, Alexa 568
	647	Allophycocyanin, Cy5, TOPRO-3
Red diode	635	Allophycocyanin, Cy5, TOPRO-3
Helium-cadmium (HeCd)	325	Indo-1, propidium iodide
	442	Mithramycin, chromomycin A3, ECFP

Wavelengths Associated with Various Light Sources ("Flow Cytometry First Principles," second edition by Alice Longobardi Givan, Wiley-Liss Publishers, 2001, page 64)

e. Claim 2: "barcode adapted to be interrogated." A specific embodiment of the claimed invention describing how a bar code may be affixed to a cylinder adapted to be rotated in accordance with the invention is described in Example 7 at page 7, lines 12-15. It is further believed that the ubiquity of bar code usage in the United States in general, and in the medical and medical diagnosis fields in particular, makes any further detailed description unnecessary. As for the term "adapted," it is well known in the art that there are various types of barcodes – the specific type of barcode selected for any given application being a function of the goals of the user – any one of which may be adapted for use with the

claimed cytometric device. (See, for example, http://www.barcodehq.com/primer.html describing barcode fundamentals.)

f. Claim 11: "a rotating means further adapted to sequentially rotate." In its ordinary meaning, "sequential" means "of, relating to, or arranged in a sequence: serial" and "following in sequence." (Merriam-Webster's Collegiate Dictionary on-line at http://www.m-w.com/home.htm.) Thus, the plain and ordinary meaning of the phrase "sequentially rotated in two directions" means rotated in a first direction and then in a second direction. One reason for doing this is to agitate the measured sample. See, for instance, Example 13 at page 10, lines 15-17 and Example 14 at page 10, lines 20-23. Thus, the phrase "adapted to sequentially rotate" is clear on its face and, further, in light of the specification.

g. Claim 13: "a cap adapted to seal the open end." In the described specific embodiments, a cap to seal a container comprises a cell guide mechanism. See, for example, page 2, lines 13-16 and page 3, lines 4-18. However, nowhere is the invention limited to a cap that includes such a mechanism. Specifically, the cell guide mechanism is explicitly noted as being "optional" at page 3, line 4 of the specification. Accordingly, any cap or other mechanism that can be adapted or conformed to create a closed container that may be rotated about its vertical axis properly falls within the ambit of the pending claims.

h. Claims 23, 27: "light emitting diode adapted to emit." It is respectfully submitted that the primary function of a light emitting diode is to emit light. (See, for

example, the online technical dictionary "Hyperdictionary" at http://www.hyperdictionary.com. A search for "light emitting diode" returns the following definition: "a type of diode that emits light when current passes through it. Depending on the material used the colour can be visible or infrared.") It is further respectfully submitted that the claimed adaptation may be for any number of technical reasons such as, but without limitation, to the specific frequency of the light desired. This would, of course, depend upon the specific use and/or tests the claimed device would be used for. Such decision being one of design choice and well within the skill of the ordinary practitioner in the field of cytometric device design.

In addition to the above specific descriptions, the use of "adapted to" language has long been accepted by the Patent Office. See M.P.E.P. 2173.05(g), *citing In re Venezia*, 530 F.2d 956 (CCPA 1976). As further evidence of the widespread, accepted and non-vague nature of this claim language, a search of the US Patent database reveals that more than thirty five (35) patents directed to cytometric methods and/or devices using the "adapted to" terminology have been issued.[1] By way of example only, the Board is directed to the following *issued* patents: **(1)** 6,658,357 – independent claim 18 is directed to a flow analyzer (i.e., cytometer) "having a plurality of data

storage areas that are adapted to receive and store incoming data;" **(2)** 6,597,438 – independent claim 10 is directed to a wearable cytometer having "a housing adapted to receive the removable cartridge;" **(3)** 6,544,770 – independent claim 1 is directed to a virus quantitation system "comprising a light source adapted for directing light along a light path;" **(4)** 6,372,506 – independent claim 1 is directed to a cytometer having "a first detector adapted to detect;" **(5)** 6,181,319 – independent claim 11 is directed to a cytometric device having "a measuring device adapted to measure a plurality of particles;" **(6)** 6,110,427 – independent claim 1 is directed to a flow regulator comprising "a chamber ... [having] ... inlet and outlet ports ... adapted to direct fluid into and out of the chamber:" **(7)** 5,726,751 – dependent claim 2 is directed to a flow module for use with a flow cytometer, wherein the flow module is "adapted for use with a particle-containing fluid;" **(8)** 5,726,404 – dependent claim 15 is directed to a liquid microswitch having an optical flow sensor "wherein said optical flow sensor is adapted to sensing light scattering from particles;" **(9)** 5,040,890 – independent claim 1 is directed to a flow cytometer flow control device having "a differential pressure transducer ... adapted for fluid communication;" and **(10)** 4,710,635 – independent claim 1 is directed to a flow cytometer having "a second excitation light source ... adapted to be driven by the energy of ... for producing a second beam of light."

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1. A search for the terms "adapted" and "cytom!" appearing in the claims of utility patents identified 36 patents. This search was performed using the Lexis/Nexis research system on 11 January 2004 by the below signed attorney.

In light of the specification, established case law and Patent Office procedure it is submitted that use of the term "adapted" would be clear to those of ordinary skill in the art having the benefit of Appellant's specification and, as such, define the claimed invention in distinct and clear enough terms to meet the requirements of 35 U.S.C. 112, second paragraph. Accordingly, it is respectfully requested that the Board withdraw the Examiner's rejection.

B. The Phrase "Cytometric Characteristic Of A Sample" Is Not Indefinite To One Of Ordinary Skill In The Art Of Flow Cytometry And Cytometric Analysis

With respect to the Examiner's rejection of independent claims 1 and 10 based on use of the term "cytometric characteristic of a sample," Appellant contends that this phrase has an accepted meaning within the field of cytometry and would be well-known to any practitioner of ordinary skill. By way of example only, and as provided to the Examiner in Appellant's Reply dated 29 January 2003, the International Society for Analytical Cytology describes cytometry in the following manner:

> The scope of Cytometry embraces all aspects of analytical cytology, which is defined broadly as characterization and measurement of cells and cellular constituents for biological, diagnostic, and therapeutic purposes. It includes components of cytochemistry, cytophysics, cell biology, molecular biology, physiology, pathology, image analysis, statistics, instrumentation, clinical laboratory practice, and other relevant subjects. (Definition obtained from *Cytometry* web site - http://www.interscience.wiley.com/jpages/0196-

4763/aims.html. *Cytometry* is the official journal of the International Society for Analytical Cytology.)

Similarly, the Clinical Flow Cytometry Society defines cytometry in the following manner (this information was also provided to the Examiner in Appellant's Reply dated 29 January 2003):

> Cytometry is the measurement (-metry) of cells (cyto-) by an analytical device (cytometer) using lasers and light detectors to determine characteristics of the cells. A flow cytometer measures these cellular properties by running the cells, suspended in a liquid, through a laser beam and the light is detected by diodes and photomultiplier tubes. An image cytometer measures the cells on a slide by shining a laser on the cells and detecting the light by photomultiplier tubes. The cellular characteristics that can be detected by a cytometer include; relative size, granularity, and the presence or absence of biochemical structures inside and on the surface of the cells. These biochemical structures can be used to identify the types of cells being detected by the cytometer and whether these cells have certain functions or whether the cells are active, resting, dying or dead. (See http://www.cytometry.org/intro.htm.)

In addition to these well-know definitions, the specification explicitly recites several specific cytometric characteristics suitable for measurement by the claimed device. See specification at page 1, lines 13-16 (the invention can "yield information on *cell location, size, shape, cellular constituents, cell volume,* and *cell buoyancy*; and when labeled with a florescent or other marker, specific *cellular constituents, cell function,* and *genomic information.*"); page 3, lines 28-30 ("The information can be useful in determining *cell type and proportion.* Said information is essential to clinical diagnosis, research and bio/pharmaceutical manufacturing."); Example 4 at page 6,

lines 20-25 (*rare event* analysis); Example 5 at page 6, lines 28-30 (*cell biomass* determination); Example 12 at page 9, line 12 to page 10, line 8 (cell *type identification*); and Example 17, lines 2-12 (X-Y *sperm separation*).

In light of the above remarks, it is submitted that use of the term "cytometric characteristic" would be clear to those of ordinary skill in the art having the benefit of Appellant's specification and, as such, define the claimed invention in distinct and clear enough terms to meet the requirements of 35 U.S.C. 112, second paragraph. Accordingly, it is respectfully requested that the Board withdraw the Examiner's rejection.

C. 35 U.S.C. 112 Does Not Require Individual Dependent Claims To Be "Functionally" Related When They Do Not Depend From One Another

The Examiner has rejected claim 3 as "indefinite in relation to claims 1 and 4, because it is unclear what structural and functional cooperative relationship exists *between* the "calibration standards" [of claim 3] and the "photoactivated crosslinker" [of claim 4] which are both affixed to the inner wall of the transparent cylinder to sort cells" (emphasis added). See Office Action dated 7 April 2003 at page 3.

Claim 3 (depending *only* from independent claim 1) recites a transparent cylinder whose inner wall has calibration standards affixed thereon. Claim 4 (also depending *only* from independent claim 1) recites a transparent cylinder whose inner wall has a photoactivated crosslinker affixed thereon. Each of claim 3 and claim 4 recite functional connectivity between themselves and their parent claim, independent claim 1. (The

specification clearly teaches the function of the calibration standards and photoactivated crosslinkers. See, for example, the specification at: page 4, lines 1-11; Example 2 at page 6, lines 5-12; and Example 10 at page 8, lines 9-18.) This is all that is required of an apparatus claim. The below signed attorney knows of no legal or procedural requirement that logically separate dependent claims need have, or show, any functional connection between them.

In summary, the Examiner's requirement that two dependent claims be functionally related is without basis in law or logic. Accordingly, it is respectfully requested that the Board withdraw the Examiner's rejection.

D. The Examiner Improperly Rejected The Claimed "An Analog Digital Converter" Under 35 U.S.C. 112

The Examiner has rejected claim 25 under 35 U.S.C. 112 as having an improper antecedent basis problem in reciting, "an analog to digital converter." second occurrence in the claim." See Office Action date 7 April 2003 at page 4.

Appellant does not understand the basis for the Examiner's rejection. Dependent claim 25 recites "[t]he spin cytometer of claim 24, wherein the detector means further comprises a processing means for associating a location identifier with an analog to digital converter output value, the location identifier identifying a location on a surface of the transparent cylinder at which the digital to analog value was obtained." See appendix at claim 25. A clear and plain reading of this claim shows no second use of the claimed "analog to digital converter" term has been used. Instead, an "analog to

digital converter output value" was defined and a subsequent reference to this term was used, "digital to analog value." (Appellant acknowledges that the final term, "digital to analog value" may be made clearer – without modifying the claimed subject matter – if amended to read "analog to digital output value." While such amendment is acceptable to the Appellant, the Examiner has not raised this issue.)

In summary, no second use of the phrase "analog to digital converter" has been used in claim 25. Accordingly, it is respectfully requested that the Board withdraw the Examiner's rejection.

E. The Claimed Invention Is Patentable Over Cottingham In View Of Walters

The Examiner has rejected independent claims 1 and 10, and dependent claims 3, 4, 11, 13-18, 22, 24-31, 33 and 34 as allegedly being unpatentable under 35 U.S.C. 103(a) over Cottingham in view of Walters.

1. Section 103 Legal Principles

A combination rejection requires three elements. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991); M.P.E.P. 2143. The first criteria is that there must be some suggestion or motivation to make the combination. Secondly, there must be a reasonable expectation of success. Thirdly, the prior art references must teach or suggest all the claimed elements. "Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Vaeck*, 947 F.2d

488, 493 (Fed. Cir. 1991), *citing In re Dow Chemical Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988).

"The mere fact that references *can be combined or modified* does not render the resultant combination obvious *unless the prior art also suggests the desirability of the combination*" (emphasis added). M.P.E.P. 2143.01 *quoting In re Mills*, 916 F.2d 680, 682 (Fed. Cir. 1990); *see also In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998) (The combination of the references taught every element of the claimed invention, however without a motivation to combine, a rejection based on a *prima facie* case of obvious was held improper.). The M.P.E.P. summarizes this requirement succinctly when it states that "[t]he level of skill in the art cannot be relied upon to provide the suggestion to combine references." M.P.E.P. 2143.01 *citing Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308 (Fed. Cir. 1999).

2. Summary of Cottingham

Cottingham describes a "disposable, self-contained test unit ... for use in ... immunoassay" work. In Cottingham see, for example, the Abstract and col. 2 at lines 58-62. A key feature of Cottingham appears to be the ability to centrifuge a plurality of disposable test units/tubes at once, wherein the centrifugation occurs about an axis *perpendicular to the long axis of the container tubes*. In Cottingham see, for example, Fig. 2 and col. 6, lines 37-47.

3. Summary of Walters

Walters describes a centrifuge apparatus to rotate a fluid tube about its longitudinal axis in discrete increments and, only when this rotation is stopped, measures a characteristic of the material therein. In Walters see, for example, col. 7, lines 13-64 and FIGS. 3, 4 and 5 (describing the function of the grooves in cam 156 are to discretely rotate the sample vial) and col. 10, line 40 to col. 11, line 67 and FIGS. 9 and 10 (describing the discrete movement of the sample vial "indexing" and the fact that measurements are taken only when the sample vial is stationary with respect to the measurement light). Specifically, Walters teaches (1) centrifuging a sample vial at a first low speed to cause separation of the constituents therein, (2) rotating the sample vial at an increased speed to discretely rotate the sample vial, (3) slowing the sample vial down so that the sample vial is not rotating about its longitudinal axis, and (4) using a detector to measure a characteristic of the material inside the sample vial wherein the sample vial is stationary with respect to the illumination source and detector. Each time a sample vial in accordance with Walters is to be rotated, the preceding four steps are repeated. In Walters, see col. 10, line 40 to col. 11, line 67 and FIGS. 9 and 10 in Walters.

4. Argument

No where does Cottingham teach, describe or fairly suggest either the rotation of a sample container about its longitudinal axis or the simultaneous rotation and interrogation of a sample via a light source. Similarly, no where does Walters teach,

describe or fairly suggest rotating a sample container about its longitudinal axis during cytometric analysis.

With respect to Walters, an explicitly claimed feature of the invention is that the sample is rotated during measurement (see independent claims 1 and 10). As discussed in the specification, such rotation moves the cells (or other components) being measured to the inner surface of the sample container where they are "held" by the centrifugal force of the rotation for measurement. See the specification at, for example, page 3, lines 2-19. Accordingly, if a sample container in accordance with the claimed invention was stopped during measurement operations as taught by Walters, all of the cells (or other components) would fall to the bottom of the container under gravitational forces where after the aforementioned cytometric measurements would not be possible. Thus, Walters actually teaches away from the claimed invention. Accordingly, neither Cottingham or Walters (alone or in combination) teach or fairly suggest the claimed invention.

Even assuming the teachings of Cottingham and Walters could be combined as the Examiner suggests,[2] without either reference suggesting such combination or the likelihood that such combination would be successful[3] (which it would not as discussed above), the Examiner is simply stating that *because* the combined references include all the claimed elements it would, *ergo*, be obvious to combine them. The Examiner has

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2 Such combination explicitly rejected by Appellant for the reasons discussed above.

3 The Examiner has cited to no such suggestion within either reference.

used the claimed invention to guide her conclusion. The Court of Appeals for the Federal Circuit has held time and again that "[o]bviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination." *In re Bond*, 910 F.2d 831, 834 (Fed. Cir. 1990), *reh'g denied, quoting Carella v. Starlight Archery and Pro Line Co.*, 804 F.2d 135, 140 (Fed. Cir. 1986); *see also, e.g., In re Stencel*, 828 F.2d 751, 755 (Fed. Cir. 1987) (reversing Board holding of obviousness); *ACS Hospital Systems, Inc. v. Montefiore Hospital*, 732 F.2d 1572, 1577 (Fed. Cir. 1987) (reversing district court holding of obviousness).

Accordingly, it is respectfully requested that the Board withdraw the Examiner's rejection.

F. The Claimed Invention Is Patentable Over Anderson In View Of Walters

The Examiner has rejected independent claims 1 and 10, and dependent claims 4, 13-18, 22, 26-29, 31, 33 and 34 under 35 U.S.C. 103 over Anderson in view of Walters.

1. Summary of Anderson

Anderson is directed to a "method for separating microorganisms ... from a mixture by two dimensional centrifugation." (In Anderson, see Abstract and col. 7, lines 31-38.) Anderson appears to specifically describe special centrifugation tubes (see col. 7, line 65 to col. 8, lines 4) in which a sample is deposited along with separation disks (see col. 8, lines 42-45) and which are then spun (see col. 9, lines 7-11). Of particular

relevance, the tubes and associated methods and apparatus of Anderson (1) do not spin about their longitudinal axis (see col. 9, lines 34-40) and (2) are moved into a fixed position prior to examination (see col. 10, lines 22-28 and FIG. 5; col. 10, lines 46-49 and FIG. 6; and col. 11, lines 32-37 and FIG. 7).

2. Summary of Walters

See discussion above.

3. Argument

Nowhere does Anderson teach, describe or fairly suggest either the rotation of a sample container about its longitudinal axis or the simultaneous rotation and interrogation of a sample. As discussed above, nowhere does Walters teach, describe or fairly suggest rotating a sample container about its longitudinal axis during cytometric analysis.

In addition, nowhere in either Anderson or Walters is there a suggestion that the discrete rotation and fixed interrogation scheme of Walters be combined with the centrifuging motion and fixed position interrogation scheme of Anderson – or that such a combination would be successful. Again, the Examiner is relying on hindsight reconstruction for the motivation to combine rather than on the cited prior art. Such reliance is strictly forbidden by established case law and Patent Office procedure. See M.P.E.P. 2143.01, *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308 (Fed. Cir. 1999); *In re Bond*, 910 F.2d 831, 834 (Fed. Cir. 1986); *In re Stencel*, 828 F.2d 751, 755 (Fed. Cir.

1987); and *ACS Hospital Systems, Inc. v. Montefiore Hospital*, 732 F.2d 1572, 1577 (Fed. Cir. 1987).

Accordingly, it is respectfully requested that the Board withdraw the Examiner's rejection.

G. The Claimed Invention Is Patentable Over Cottingham Or Anderson In View Of Walters And Further In View Of Surmodics, Inc.

The Examiner has rejected dependent claims 19, 20 and 23 as allegedly being unpatentable under 35 U.S.C. 103(a) over Cottingham or Anderson in view of Walters and further in view of Surmodics, Inc.

Each of claims 19, 20 and 23 depend from independent claim 10. Because independent claim 10 is allowable over the cited prior art for at least the reasons discussed above, each of dependent claims 19, 20 and 23 is allowable.

Accordingly, it is respectfully requested that the Board withdraw the Examiner's rejection.

H. The Claimed Invention Is Patentable Over Cottingham Or Anderson In View Of Walters And Further In View Of Saralegui

The Examiner has rejected dependent claims 2 and 21 as allegedly being unpatentable under 35 U.S.C. 103(a) over Cottingham or Anderson in view of Walters and further in view of Surmodics, Inc.

Claim 2 depends from independent claim 1 and claim 21 depends from independent claim 10 – both of which are allowable over the cited prior art for at least the reasons discussed above. Therefore, each of dependent claims 2 and 21 are allowable.

Accordingly, it is respectfully requested that the Board withdraw the Examiner's rejection.

SUMMARY AND CONCLUSIONS

In light of the aforementioned differences, Appellant submits that the claimed invention is patentably distinct over the cited prior art, and respectfully requests the Board reverse the Examiner's rejections as to all claims and allow the claims to issue.

23 JAN 2004

Date

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1. A cytometer apparatus comprising:

a rotating means adapted to receive and rotate a transparent cylinder along a longitudinal axis of the transparent cylinder;

a light source adapted to illuminate at least a portion of said transparent cylinder while the transparent cylinder is being rotated by the rotating means;

a detector adapted to detect a light signal provided by said light source and reflected from said transparent cylinder while the transparent cylinder is being rotated by the rotating means;

determining means for determining at least one cytometric characteristic of a sample disposed in said transparent cylinder based on said light signal; and

a movement means for moving said transparent cylinder and said light source and detector in a longitudinal axis relative to one another.

2. The cytometer apparatus as set forth in claim 1, wherein said transparent cylinder comprises a bar code label affixed to an outer wall thereof, said bar code label adapted to be interrogated by said detector means.

3. The cytometer apparatus as set forth in claim 1, wherein said transparent cylinder has an inner wall having calibration standards affixed thereon.

4. The cytometer apparatus as set forth in claim 1, wherein said transparent cylinder comprises an inner wall having a photoactivated crosslinker affixed thereon.

10. A spin cytometer, comprising:

a rotating means adapted to rotate a transparent cylinder about a longitudinal axis of the transparent cylinder;

a light source adapted to illuminate at least a portion of the transparent cylinder while the transparent cylinder is being rotated by the rotating means;

a detector means for detecting a light signal generated by the light source and reflected from the transparent cylinder while the transparent cylinder is being rotated by the rotating means;

determining means for determining at least one cytometric characteristic of a sample disposed in said transparent cylinder based on said detected light signal; and

a movement means for moving the transparent cylinder and the light source and detector means in relative motion.

11. The spin cytometer of claim 10, wherein the rotating means is further adapted to sequentially rotate a transparent cylinder in two (2) directions.

13. The spin cytometer of claim 10, wherein the rotating means is adapted to rotate a transparent cylinder comprising:

a closed end;

an open end;

a cell guide member having a first side oriented toward the open end, a second side oriented toward the closed end, and a passage from the first side to the second side; and

a cap adapted to seal the open end.

14. The spin cytometer of claim 13, wherein the passage is smaller at said first side than it is at said second side.

15. The spin cytometer of claim 14, wherein the passage is substantially smaller than the diameter of said transparent cylinder.

16. The spin cytometer of claim 13, wherein the closed end has a smaller outside diameter than the open end.

17. The spin cytometer of claim 13, wherein said transparent cylinder comprises a polystyrene cylinder.

18. The spin cytometer of claim 13, wherein an inner wall of said transparent cylinder comprises an organic photoreceptor material affixed thereon.

19. The spin cytometer of claim 18, wherein the organic photoreceptor material is activated by a wave length of approximately 300 nanometers to approximately 800 nanometers.

20. The spin cytometer of claim 19, wherein the organic photoreceptor material comprises dibromo anthanthrone.

21. The spin cytometer of claim 10, wherein the rotating means comprises a stepper motor.

22. The spin cytometer of claim 10, wherein the light source comprises a light emitting diode.

23. The spin cytometer of claim 22, wherein the light emitting diode is adapted to emit a light having a wavelength of between approximately 300 nanometers and 800 nanometers.

24. The spin cytometer of claim 10, wherein the detector means further comprises an analog to digital converter.

25. The spin cytometer of claim 24, wherein the detector means further comprises a processing means for associating a location identifier with an analog to digital converter output value, the location identifier identifying a location on a surface of the transparent cylinder at which the digital to analog value was obtained.

26. The spin cytometer of claim 10, further comprising an additional one (1) or more light sources, each light source adapted to illuminate at least a portion of the transparent cylinder.

27. The spin cytometer of claim 26, wherein each of the additional one (1) or more light sources are adapted to emit a different wavelength.

28. The spin cytometer of claim 10, further comprising at least one diffraction grating.

29. The spin cytometer of claim 10, wherein the detector means comprises a photomultiplier.

30. The spin cytometer of claim 10, wherein the detector means comprises a charge coupled device.

31. The spin cytometer of claim 27, further comprising an additional one (1) or more detector means, each detector means responsive to a light signal generated by one of the light sources.

33. The spin cytometer of claim 10, wherein the movement means moves the transparent cylinder in a direction substantially parallel to the transparent cylinder's longitudinal axis.

34. The spin cytometer of claim 10, wherein the movement means moves the light source and detector means in a direction substantially parallel to the transparent cylinder's longitudinal axis.